American Journal of Medical Genetics 70:28–31 (1997)

Brief Clinical Report

Bruck Syndrome (Osteogenesis Imperfecta With Congenital Joint Contractures): Review and Report on the First North American Case

Elizabeth McPherson* and Michele Clemens
University of Pittsburgh and Magee-Womens Hospital, Pittsburgh, Pennsylvania

We describe a patient who was born with flexion contractures and pterygia at the elbows, clubfeet, torticollis, and several rib fractures. During infancy and childhood, multiple fractures of the lower limbs occurred with minimal trauma and led to disabling deformities. When evaluated at age 19 years, he was normally intelligent, but extremely short, with severe kyphoscoliosis compromising his pulmonary function. Pterygia limited elbow extension to 90°, and severe lower limb deformities prevented ambulation. He did not have blue sclerae, dentinogenesis imperfecta, or hearing loss. X-ray studies showed demineralized bones, severe deformity and cystic change at old fracture sites, and vertebral wedging. Collagen studies on skin fibroblasts were normal. Am. J. Med. Genet. 70:28–31, 1997.

KEY WORDS: osteogenesis imperfecta; arthrogryposis; contractures; pterygia; collagen

INTRODUCTION

The combination of multiple joint contractures and osteogenesis imperfecta was first recognized by Bruck [1897]. Since that time, only 7 additional patients have been described: 1 from India [Sharma and Anand, 1964], 5 from South Africa [Viljoen et al., 1989], and 1 from Europe [Brenner et al., 1993]. All except Bruck's original patient were documented to have clubfeet and flexion contractures of the knees and/or elbows at birth. The photograph of Bruck's patient suggests a pterygium at the axillae, and with the possible exception of the patient of Sharma and Anand [1964] who is described only briefly without photographs, all subsequent patients have had antecubital and/or popliteal pterygia. Onset of fractures, often after minimal trauma, ranged from birth to the teenage years, and the fractures invariably resulted in severe deformity. The patient of Sharma and Anand [1964] was noted at age 6 weeks to have blue sclerae, knee flexion contractures, a clubfoot, and old fractures of the femora, humerus, and clavicles. Because she died of infection, no follow-up was possible. All surviving patients had white sclerae when first examined, but none were evaluated for osteogenesis imperfecta as infants. All developed postnatal short stature and progressive kyphoscoliosis. One adolescent had cleft soft palate and "mild dentinogenesis imperfecta." All have had normal hearing and normal intelligence. No anomalies of the skin or internal organs have been reported.

We describe a 19-year-old man with a similar history of "arthrogryposis" at birth, followed by frequent fractures and progressive deformity.

CLINICAL REPORT

K.G. was the product of an uncomplicated pregnancy to a 30-year-old gravida 2 mother. He was born by breech vaginal delivery at 36 weeks of gestation, with a birth weight of 2,200 g (25th centile). Radiographs in the neonatal period showed a fracture of the right femur and several old rib fractures (Fig. 1a,b). He was noted to have "arthrogryposis multiplex congenita" with flexion contractures and pterygia at the elbows, adducted thumbs, bilateral equinovarus feet, and torticollis. He was treated primarily with physical therapy and splinting. At age 1 month, bilateral inguinal hernias were repaired. During infancy and childhood, he suffered many additional fractures with minimal trauma. These healed with deformity and cystic changes. He was diagnosed with "osteogenesis imperfecta," but no type was ever specified. He was noted to have decreased muscle mass, severe osteoporosis, and progressive kyphoscoliosis. He never walked independently. His language, cognitive, and fine motor skills were normal.

When examined at age 19 years he was approximately 122 cm long with an arm span of 162.5 cm. His short stature was attributable to severe kyphoscoliosis and lower limb deformities with angulated femora and

*Correspondence to: Elizabeth McPherson, M.D., Department of Genetics, Magee-Womens Hospital, 300 Halket Street, Pittsburgh, PA 15213.

Received 6 January 1996; Accepted 3 September 1996

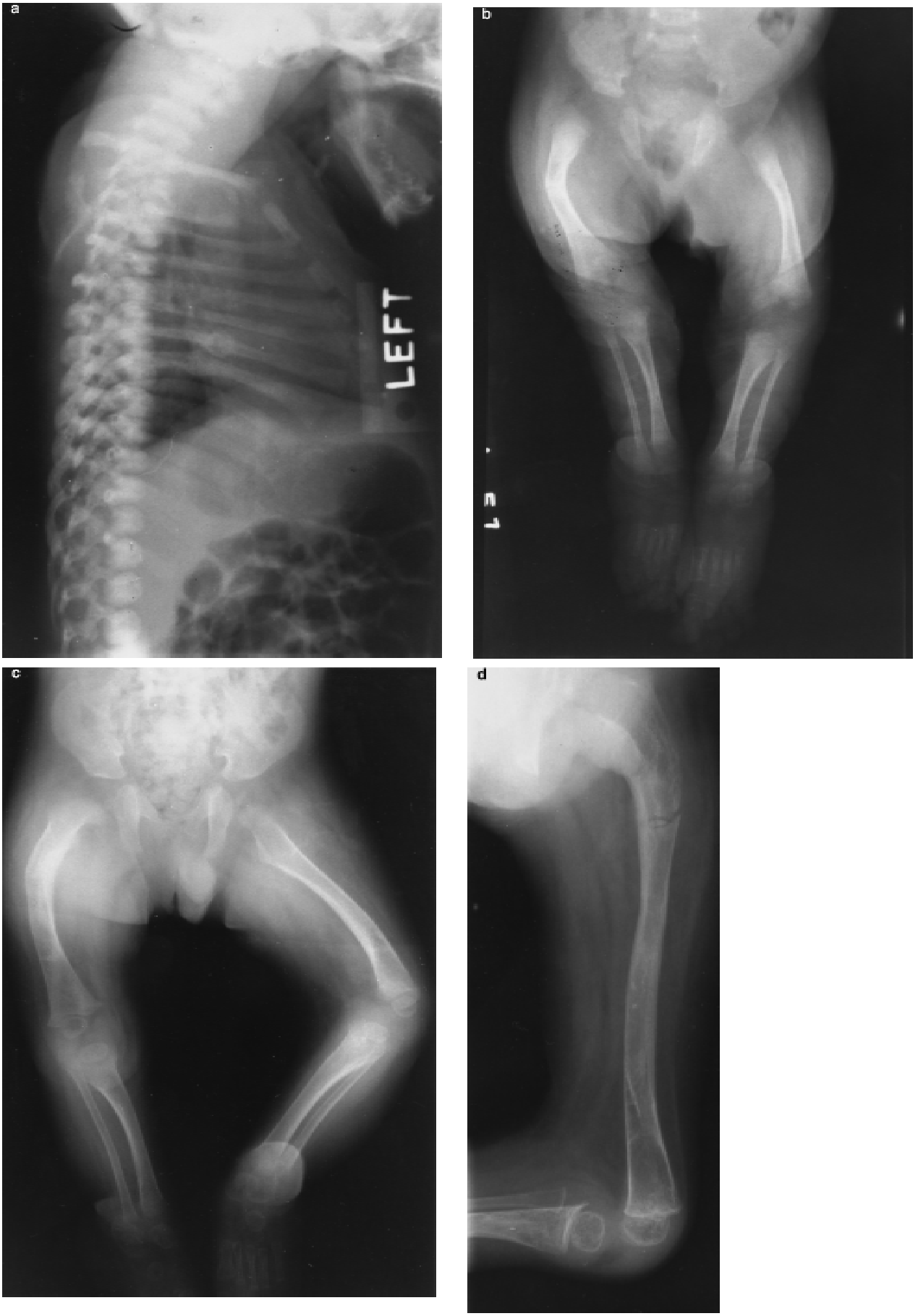

Fig. 1. Legend on overleaf.

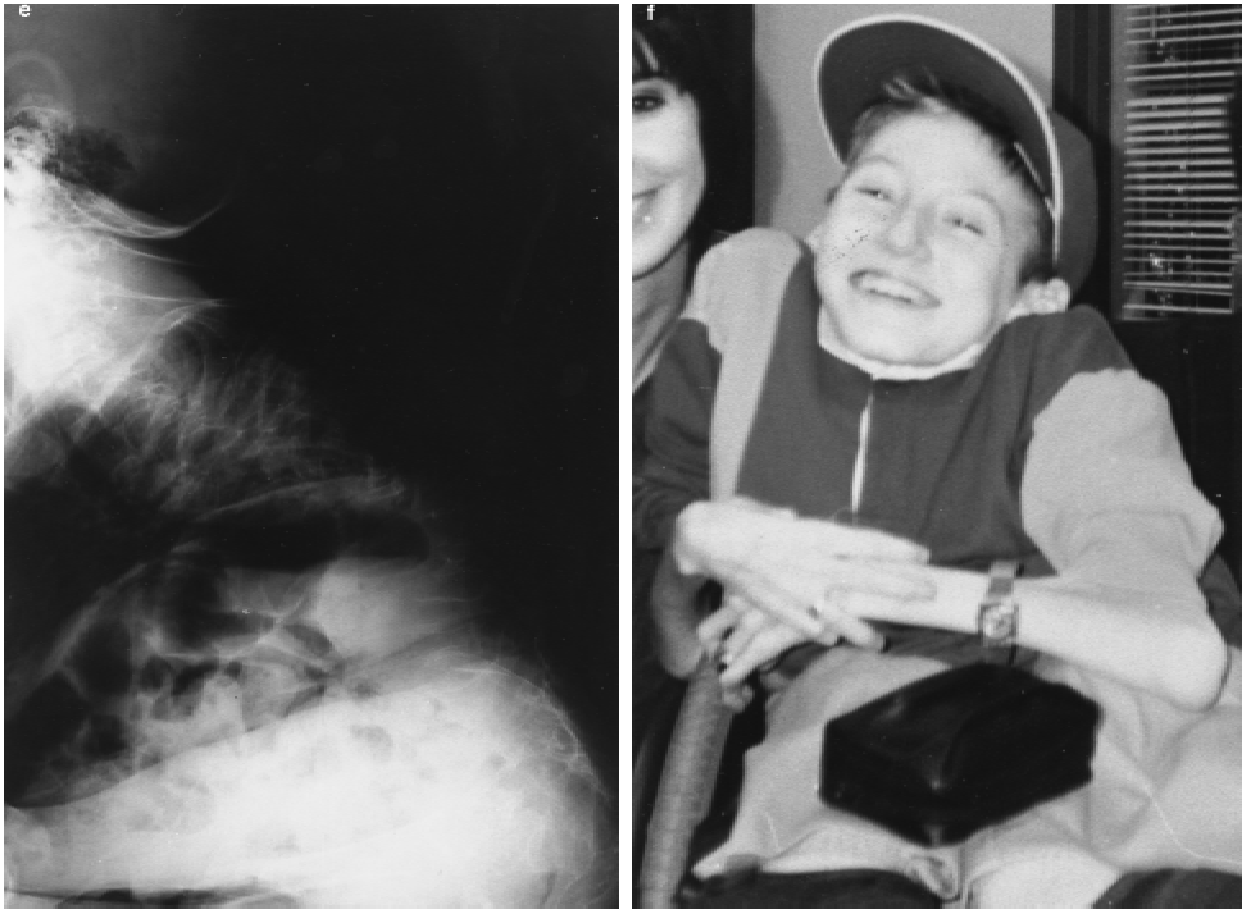

Fig. 1. **a:** Lateral neonatal chest film showing healing rib fractures and relatively normal spine. **b:** Lower limbs studied neonatally, with fracture of right femur, slight bowing of right tibia and left femur, equinovarus feet, and mild flexion contracture of left knee. **c:** Lower limbs at age 9 months, showing healing of right femur with angulation and exacerbation of knee flexion contractures. **d:** Left lower limb at age 4 years, showing angulation and cystic change at old fracture sites in proximal femur and tibia, new fracture of femur, osteoporosis, and severe knee flexion contracture. **e:** Lateral spine at age 13 years, showing severe kyphoscoliosis, wedge vertebrae, and osteoporosis. A few wormian bones seen on the original of this film show poorly in reproduction. **f:** Patient as an adolescent, showing essentially normal face, severe kyphoscoliosis, reduced muscle mass, and pterygium of the elbow.

saber shins. His muscle mass was minimal, and he had virtually no mobility of the lower limbs due to chronic pain and contractures. A recent fracture of his right humerus, sustained when he tried to turn the steering wheel during driver training, had healed with severe angulation. His elbow extension was limited by pterygia to 90° (Fig. 1f). Despite adducted thumbs he had good use of his hands. He had bridged palmar creases on the left and a Sydney line on the right. His torticollis had resolved. He had pectus carinatum and restrictive lung disease related to scoliosis. Heart sounds were normal. Strength was normal despite diminished muscle mass. His head circumference was 54.5 cm and except for mild asymmetry due to asynclitism, he had a normal facial appearance. His sclerae were white. His vision and hearing were normal. He had mild pitting of his dental enamel but no evidence of dentinogenesis imperfecta. His skin texture and healing of surgical incisions were normal. He died at age 21 of restrictive lung disease.

Review of old radiographs showed gracile bones with severe generalized osteoporosis, wedged vertebrae, cystic lesions and deformity at old fracture sites, and a few wormian bones (Fig. 1c–e). He declined additional radiographic studies but agreed to a skin biopsy. Collagen studies of skin fibroblasts showed none of the changes commonly found in osteogenesis imperfecta.

The parents of K.G. are healthy and non-consanguineous. An older sister is clinically normal, and there is no family history suggestive of either arthrogryposis or osteogenesis imperfecta.

DISCUSSION

The association of congenital contractures, primarily of the elbows, knees, and ankles, with severe bony fragility constitutes a syndrome which can be distinguished from all major subtypes of osteogenesis imperfecta and the more common forms of arthrogryposis. The term “Bruck syndrome” has been applied to this entity, although Bruck’s original patient apparently did not have congenital contractures and may have had a different condition. Excluding Bruck’s patient, all patients have had congenital contractures with pterygia, onset of fractures in infancy or early childhood, postnatal short stature, severe limb deformity, and progressive kyphoscoliosis. All have been normally intelligent, with normal vision and hearing. Most have had

white sclerae and normal teeth. Since the contractures are congenital and associated with pterygia, while the fractures are often of postnatal onset, the contractures must be considered a primary abnormality and cannot be a complication of the fractures or the resulting immobilization. Furthermore, most children with other forms of osteogenesis imperfecta have hyperextensible joints. Although children with other forms of arthrogryposis may develop osteoporosis due to immobility and may suffer pathologic fractures, these are never as frequent or as progressively deforming as those observed in the reported Bruck syndrome patients. Thus, the fractures must also be considered a primary finding of Bruck syndrome. Because a set of 3 affected sibs, including the only female patient, was reported by Viljoen et al. [1989], Bruck syndrome is thought to be an autosomal-recessive trait, although all other cases have been sporadic. The underlying biochemical abnormality remains unknown, and there have been no attempts to map the gene.

Brenner et al. [1993] considered Bruck syndrome a form of osteogenesis imperfecta because they found morphological and biochemical abnormalities of collagen in bone from their patient. Morphologically, they noted mixed callus with variable thickness of osteoid, similar to that seen in other forms of osteogenesis imperfecta. Electron microscopy showed osteoblasts with swollen mitochondria and dilated endoplasmic reticulum. There was variation in diameter of the collagen fibrils with a mean diameter of 428 ± 86 A in their patient, compared to 560 ± 37 A in controls. Biochemical studies showed low mineral content and increased pepsin extraction of collagen I. The size of the apatite crystals was increased rather than decreased, as in other forms of osteogenesis imperfecta. We were not able to examine a bone specimen from our patient, but shortly before his death, we obtained skin fibroblasts. Our patient differed from most individuals with any of the common forms of osteogenesis imperfecta in that his cells demonstrated no abnormality of type I or type III procollagen or collagen structure or synthesis. Because detailed sequence analysis of COL1A1 and COL1A2 has not been carried out, the possibility of a subtle structural alteration of collagen has not been excluded completely.

ACKNOWLEDGMENTS

We thank Dr. Peter Byers for the collagen studies on fibroblasts from our patient. Also, we thank our patient (posthumously) and his family for their help in this investigation.

REFERENCES

Brenner RE, Vetter U, Stoss H, Muller PK, Teller WM (1993): Defective collagen fibril formation and mineralization in osteogenesis imperfecta with congenital joint contractures. Eur J Pediatr 152:505–508.

Bruck A (1897): Ueber eine seltene Form von Erkrankung der Knochen und Gelenke. Dtsch Med Wochenschr 23:152–155.

Sharma NL, Anand JS (1964): Osteogenesis imperfecta with arthrogryposis multiplex congenita. Indian Med J 53:124–126.

Viljoen D, Versfeld G, Beighton P (1989): Osteogenesis imperfecta with multiple joint contractures. Clin Genet 36:122–126.